Express Mail No. EM180791250US

PTO/SB/08A (08-03)

Approved for use through 07/31/2006. OMB 0651-0031

U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449/PTO Complete if Known INFORMATION DISCLOSURE 10/562,089 **Application Number** Filing Date **December 23, 2005** STATEMENT BY APPLICANT First Named Inventor Catherine Lofton-Day (Use as many sheets as necessary) **Art Unit** 2161 **Examiner Name** Not yet assigned 4 47675-165 of **Attorney Docket Number** Sheet

			U.S.	PATEN	T DOCUME	ENTS		
Examiner	Cite	Document Number	Publication Date		Name of Patentee or		Pages, Columns, Lines, Where Relevant Passages or Relevant	
Initials*	No. ¹	Number-Kind Code ¹ (if known)	MM-DD-Y			olicant of Cited Document	Figures Appear	··
		US- 5565552	10-15-199					
		US- 5567810	10-22-1996		Weis et al			
		US- 5574142	11-12-1996		Meyer, Jr.	et al.		
		US- 5585481	12-17-1996 A		Arnold, Jr.	et al.		
		US- 5587371	12-24-199	12-24-1996 Sessier et al.				
		US- 5597696	01-28-199	7	7 Linn et al.			
		US- 5786146	07-28-199	8	Herman et al.		<u> </u>	
		US- 5958773	09-28-199	9	Monia et al.			
		US- 6251594	06-26-200)1	Gonzalgo et al.			
		US- 6265171	07-24-200	1 Herman et al.		t al.		
		US- 6331393	12-18-200	2-18-2001 Laird et al.				
		US- 10/603,138	06-23-200	003 Lofton-Day		y et al.		,
	1		FOREIC	SN PAT	ENT DOCU	MENTS		
Examiner Initials*	Cite No.1	Foreign Patent Document Country Code ³ -Number ⁴ -Kind Code			ation Date	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages Or Relevant Figures Appear	
Hillais		WO 95/00669	95/00669		I-05-1995 Pharmacia Biotech AB			
		WO 95/15373			08-1995 McGill University			
	-	WO 97/46705			1997	Johns Hopkins		
		WO 99/28498		06-10-		Epigenomics GmbH		
		WO 00/26401			2000	Johns Hopkins		
		WO 01/75172		10-11-	2001	University of Southern California		
								
	 -			 				

Date Examiner Signature Considered

EXAMINER: Initial if reference considered, whether or not citation is in conformation with MPEP 609. Draw line through citation if not in conformation and not considered. Include copy of this form with next communication to applicant. Applicant's unique citation designation number (optional). See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04 Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. Kind of document by the appropriate symbols as indicated on the document under WIPO Standard St. 16 if possible. Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to compete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450. If you need assistance in completing the form, call 1-800-PTO-9199 (1-800-786-9199) and select option 2.

Express Mail No.EM180791250US

47675-165

PTO/SB/08A (08-03)

Approved for use through 07/31/2006. OMB 0651-0031

U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Complete if Known Substitute for form 1449/PTO 10/562,089 INFORMATION DISCLOSURE **Application Number** December 23, 2005 Filing Date STATEMENT BY APPLICANT Catherine Lofton-Day First Named Inventor 2161 (Use as many sheets as necessary) Art Unit Not yet assigned **Examiner Name**

Sheet

Attorney Docket Number

		NON PATENT LITERATURE DOCUMENTS	<u> </u>
Examiner nitials*	Cite No. 1	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T²
		BACHMAN et al., "Methylation-associated Silencing of the Tissue Inhibitor of Metalloproteinase-3 Gene Suggests a Suppressor Role in Kidney, Brain, and Other Human Cancers," Cancer Research, February 15, 1999, Volume 59	,
		DATABASE, "H. sapiens CpG island DNA genomic Msel fragment, clone 97b5, forward read cpg97b5.ftla," XP002312906, retrieved from EBI accession no. EM_HUM:HS97B5F, October 23, 1995 (1 page)	
,		EADS et al., "CpG Island Hypermethylation in Human Colorectal Tumors Is Not Associated with DNA Methyltransferase Overexpression," Cancer Research, May 15, 1999, pp. 2302-2306, Volume 59	
-		EADS et al., "Epigenetic Patterns in the Progression of Esophageal Adenocarcinoma," Cancer Research, April 15, 2001, pp. 3410-3418, Volume 61	
		EADS et al., "Fields of Aberrant CpG Island Hypermethylation in Barrett's Esophagus and Associated Adenocarcinoma," Cancer Research, September 15, 2000, pp. 5021-5026, Volume 60	
		FEIL et al., "Methylation analysis on individual chromosomes: improved protocol for bisulphite genomic sequencing," Nucleic Acids Research, 1994, pp. 695-696, Volume 22, Number 4	
		FROMMER et al., "A genomic sequencing protocol that yields a positive display of 5-methylcytosine residues in individual DNA strands," The Proceedings of the National Academy of Sciences, March 1992, pp. 1827-1831, Volume 89	
		GONZALGO et al., "Identification and Characterization of Differentially Methylated Regions of Genomic DNA by Methylation-sensitive Arbitrarily Primed PCR," Cancer Research, February 15, 1997, pp. 594-599, Volume 57	
		GONZALGO et al., "Rapid quantitation of methylation differences at specific sites using methylation-sensitive single nucleotide primer extension (Ms-SNuPE), Nucleic Acids Research, 1997, pp. 2529-2531, Volume 25, Number 12	
-		GRIGG et al., "Sequencing 5-Methylcytosine Residues in Genomic DNA," BioEssays, June 1994, pp. 431-436, Volume 16, Number 6	
		GUT et al, "DNA and Matrix Assisted Laser Desorption Ionization Mass Spectrometry," Molecular Biology: Current Innovations and Future Trends, 1995, pp. 147-157, Horizon Scientific Press, Wymondham, United Kingdom	
<u>-</u>		GUT et al., "A procedure for selection DNA alkylation and detection by mass spectrometry," Nucleic Acids Research, 1995, pp. 1367-1373, Volume 23, Number 8	
·		HEID et al., "Real Time Quantitative PCR," Genome Research, 1996, pp. 986-994, Volume 6	
		HERMAN et al., "Inactivation of the CDKN2/p16/MTS1 Gene Is Frequently Associated with Aberrant DNA Methylation in All Common Human Cancer," Cancer Research, October 15, 1995, pp. 4525-4530, Volume 55	
		HERMAN et al., "Methylation-specific PCR: A novel PCR assay for methylation status of CpG islands," The Proceedings of the National Academy of Sciences, September 1996, pp. 9821-9826, Volume 93	
		HILTUNEN et al., "Hypermethylation of the APC (Adenomatous Polyposis Coli) Gene Promoter Region in Human Colorectal Carcinoma," The International Journal of Cancer, 1997, pp. 644-648, Volume 70	
		KARAS et al., "Laser Desorption Ionization of Proteins with Molecular Masses Exceeding 10 000 Daltons," Analytical Chemistry, October 15, 1988, pp. 2299-2301, Volume 60, Number 20	

Date Examiner Signature Considered

EXAMINER: Initial if reference considered, whether or not citation is in conformation with MPEP 609. Draw line through citation if not in conformation and not considered. Include copy of this form with next communication to applicant. Applicant's unique citation designation number (optional). See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04 ³ Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). 4 For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. 5 Kind of document by the appropriate symbols as indicated on the document under WIPO Standard St. 16 if possible. 6 Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to compete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 (1-800-786-9199) and select option 2.

Express Mail No.EM180791250US

PTO/SB/08A (08-03)

Approved for use through 07/31/2006. OMB 0651-0031

U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449/PTO

Sheet

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

of

(Use as many sheets as necessary)

Co	mplete if Known	
Application Number	10/562,089	
Filing Date	December 23, 2005	
First Named Inventor	Catherine Lofton-Day	
Art Unit	2161	
Examiner Name	Not yet assigned	
Attorney Docket Number	47675-165	

		NON PATENT LITERATURE DOCUMENTS	,
Examiner Initials*	Cite No.1	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T²
		MARTIN et al., "Genomic sequencing indicates a correlation between DNA hypomethylation in the 5' region of the pS2 gene and its expression in human breast cancer cell lines," Gene, 1995, pp. 261-265, Volume 157	
		OLEK et al., "A modified and improved method for bisulphite based cytosine methylation analysis," Nucleic Acids Research, 1996, pp. 5064-5066, Volume 24, Number 24	
		OLEK et al., "The pre-implantation ontogeny of the H19 methylation imprint," Nature Genetics, November 1997, pp. 275-276, Volume 17	
		REIN et al., "Identifying 5-methylcytosine and related modifications in DNA genomes," Nucleic Acids Research, 1998, pp. 2255-2264, Volume 26, Number 10	!
		SADRI et al., "Rapid analysis of DNA methylation using new restriction enzyme sites created by bisulfite modification," Nucleic Acids Research, 1996, pp. 5058-5059, Volume 24, Number 24	
		SANGER et al., "DNA Sequencing with chain-terminating inhibitors," The Proceedings of the National Academy of Sciences, December 1977, pp. 5463-5468, Volume 74, Number 12	
		TOYOTA et al., "CpG island methylator phenotype in colorectal cancer," The Proceedings of the National Academy of Sciences, July 1999, pp. 8681-8686, Volume 96	
-		TOYOTA et al., "Identification of Differentially Methylated Sequences in Colorectal Cancer by Methylated CpG Island Amplification," Cancer Research, May 15, 1999, pp. 2307-2312, Volume 59	= .
		VAN DER KROL et al., "Modulation of Eukaryotic Gene Expression by Complementary RNA or DNA Sequences," BioTechniques, 1988, pp. 958-976, Volume 6, Number 10	
		VAN RIJNSOEVER et al., "Characterisation of colorectal cancers showing hypermethylation at multiple CpG islands," Gut, 2002, pp. 797-802, Volume 51	
		XIONG et al., "COBRA: a sensitive and quantitative DNA methylation assay," Nucleic Acids Research, 1997, pp. 2532-2534, Volume 25, Number 12	
·		YAN et al., "CpG Island Arrays: An Application toward Deciphering Epigenetic Signatures of Breast Cancer," Clinical Cancer Research, April 2000, pp. 1432-1438, Volume 6	
		YOUNG et al., "HPP1: A transmembrane protein-encoding gene commonly methylated in colorectal polyps and cancers," The Proceedings of the National Academy of Sciences, January 2, 2001, pp. 265-270, Volume 98, Number 1	
		YU et al., "Specific Inhibition of PCR by Non-Extendable Oligonucleotides Using a 5' to 3' Exonuclease-Deficient DNA Polymerase," BioTechniques, 1997, pp. 714-720, Volume 23, Number 4	
		ZESCHNIGK et al., "Imprinted segments in the human genome: different DNA methylation pattersn in the Prader-Willi/ Angelman syndrome region as determined by the genomic sequencing method," Human Molecular Genetics, 1997, pp. 387-395, Volume 6, Number 3	
		ZESCHNIGK et al., "A single-tube PCR test for the diagnosis of Angelman and Prader-Willi syndrome based on allelic methylation differences at the SNRPN locus," European Journal of Human Genetics, March-April 1997, pp. 94-98, Volume 5, Number 2	

Examiner Signature	Date	
	Considered	

EXAMINER: Initial if reference considered, whether or not citation is in conformation with MPEP 609. Draw line through citation if not in conformation and not considered. Include copy of this form with next communication to applicant. 1 Applicant's unique citation designation number (optional). 2 See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04 3 Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). 4 For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵ Kind of document by the appropriate symbols as indicated on the document under WIPO Standard St. 16 if possible. ⁶ Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to compete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandra, VA 22313-1450. If you need assistance in completing the form, call 1-800-PTO-9199 (1-800-786-9199) and select option 2.

Express Mail No.EM180791250US

PTO/SB/08A (08-03)

Approved for use through 07/31/2006. OMB 0651-0031

U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Complete if Known Substitute for form 1449/PTO INFORMATION DISCLOSURE **Application Number** 10/562,089 Filing Date **December 23, 2005** STATEMENT BY APPLICANT First Named Inventor Catherine Lofton-Day (Use as many sheets as necessary) **Art Unit** 2161 Not yet assigned **Examiner Name** 47675-165 Sheet

Attorney Docket Number

of

		NON PATENT LITERATURE DOCUMENT	S		
Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when approp serial, symposium, catalog, etc.), date, page(s), v number(s), publisher, city and/or country where	oriate), title of the		T²
		ZON, "Oligonucleotide Analogues as Potential Chemotherapeutic Agents," Pl 549, Voume 5, Number 9	harmaceutical l	Research, 1988, pp. 539-	
7				•	ì
			·	· · · · ·	
			·		
	· · · · · · · · · · · · · · · · · · ·				
				-	
				· · · · · · · · · · · · · · · · · · ·	
			•		
	·				
					
					
, 					
**************************************					_
Examiner Signature		-	Date Considered		

EXAMINER: Initial if reference considered, whether or not citation is in conformation with MPEP 609. Draw line through citation if not in conformation and not considered. Include copy of this form with next communication to applicant. Applicant's unique citation designation number (optional). 2 See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04 3 Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). 4 For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. 5 Kind of document by the appropriate symbols as indicated on the document under WIPO Standard St. 16 if possible. 6 Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to compete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450. If you need assistance in completing the form, call 1-800-PTO-9199 (1-800-786-9199) and select option 2.